PARTICLE FORMATION AND MORPHOLOGY

RELATED APPLICATION(S)

[0001] This application is a continuation of International Application No. PCT/US2020/015957, filed on Jan. 30, 2020, published in English, which claims the benefit of U.S. Provisional Application No. 62/799,696, filed on Jan. 31, 2019. The entire teachings of the above applications are incorporated herein by reference.

TECHNICAL FIELD

[0002] The present disclosure relates to compositions and methods that enable the formation of pharmaceutically relevant particles that can be used for therapy. In particular, the methods disclosed herein allow the formation of circular particles having low internal void spaces comprising bioactive therapeutic agents.

BACKGROUND

[0003] Materials science and the application of nanotechnology calls for more efficient, reproducible and innovative technologies to synthesize novel functional particles. Recent advances in synthesis and the controlled assembly of bioactive particles have enabled their applications for use in therapy. Current efforts have been directed to developing new synthetic approaches for non-circular microparticles that often exhibit physical properties unobtainable by simply tuning the size and form of the particles. However, the application of these techniques to circular particles have been limited due to the lack of sufficient control over size uniformity, shape selectivity, surface functionality and skeletal density of the particles which are often difficult to obtain. Therefore, a highly robust and controlled method for circular particle preparation is needed.

SUMMARY

[0004] Provided herein is a particle, or a composition comprising a plurality of particles, comprising an agent, wherein the particle comprises less than about 25% internal void spaces and the circularity of the particle is from about 0.10 to about 1.00.

[0005] In one aspect, the disclosure provides a particle comprising an agent, wherein the particle comprises less than about 25% internal void spaces and the circularity of the particle is from about 0.10 to about 1.00.

[0006] In another aspect, the disclosure provides a composition comprising a plurality of particles comprising an agent suspended in a liquid, wherein the particles comprise less than about 25% internal void spaces and the circularity of the particles are from about 0.10 to about 1.00.

[0007] The present disclosure also provides a method of forming particles.

[0008] In one aspect, the disclosure provides a method of forming particles, the method comprising:

[0009] a) providing droplets comprising a first liquid and an agent;

[0010] b) contacting the droplets with a second liquid;

[0011] c) allowing the droplets to dry; and

[0012] d) removing the first and second liquids,

thereby forming particles comprising an agent, wherein the particles comprise less than about 25% internal void spaces and the circularity of the particles is from about 0.10 to about 1.00 after removing the first and second liquids.

[0013] Also provided herein, is a method of controlling the morphology of particles.

[0014] In one aspect, the disclosure provides a method of controlling the morphology of particles, the method comprising:

[0015] a) providing droplets comprising a first liquid and an agent;

[0016] b) contacting the droplets with a second liquid under a specified Peclet number;

[0017] c) allowing the droplets to dry; and

[0018] d) removing the first and second liquids,

[0019] wherein the specified Peclet number controls the morphology of the particles.

[0020] The present disclosure also provides herein a method of controlling the surface properties of particles.

[0021] In one aspect, the disclosure provides a method of controlling the surface properties of particles, the method comprising:

[0022] a) providing droplets comprising a first liquid, a first component, and a second component, wherein the first component is present in an amount closer to its solubility limit than the second component, the first component has a higher Peclet number than the second component, or a combination thereof;

[0023] b) contacting the droplets with a second liquid;

[0024] c) allowing the droplets to dry; and

[0025] d) removing the first and second liquids,

[0026] thereby forming particles, wherein the first component is enriched at the surface of the particles relative to the second component.

[0027] The present compositions and methods may be useful for the formation of pharmaceutically relevant particles that can be used for therapy. In preferred embodiments, the methods disclosed herein may allow the formation of circular particles having low internal void spaces comprising bioactive therapeutic agents.

BRIEF DESCRIPTION OF THE DRAWINGS

[0028] The foregoing will be apparent from the following more particular description of example embodiments, as illustrated in the accompanying drawings in which like reference characters, refer to the same parts throughout the different views. The drawings are not necessarily to scale, emphasis instead being placed upon illustrating embodiments.

[0029] FIG. **1**A shows an image of human IgG particles produced using a second liquid for which the Peclet number substantially less than 1.

[0030] FIG. **1**B shows an image of human IgG particles produced using a second liquid for which the Peclet number was substantially higher than 1.

[0031] FIGS. **2**A-**2**C show images of human IgG particles formed through methods of the disclosure using several second liquids having varying levels of presaturation with respect to the first liquid.

[0032] FIG. **3**A shows an image of a human IgG particle surface formed through methods of the disclosure.

[0033] FIG. **3**B shows an image of a human IgG particle sectioned to reveal the internal cross-section.

[0034] FIG. **4** shows a graph of the dispersive surface energy profiles for particles formed in second liquids of varying polarity.